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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,980	09/24/2004	Ryuji Kaji	TOYA140.001APC	1114

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
KOSSON, ROSANNE	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 12/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/508,980	KAJI ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *1-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' election without traverse of Group III, claims 8-9 in the reply filed on December 2, 2005 is acknowledged. Claims 1-7 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. No claims have been amended, canceled or added. Accordingly, claims 8-9 are examined on the merits herewith.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al. (US 5,696,077). Johnson et al. disclose a method of treating muscle hyperactivity, comprising administering a purified botulinum toxin to a patient with muscle hyperactivity, the muscle hyperactivity resulting from various diseases involving involuntary muscle movements and spasms. See col. 1, lines 31-47; col. 2, lines 35-39; col. 2, line 65, to col. 3, line 6. The toxin preparation contains purified Type B toxin at a known concentration, the toxin separated from its non-toxic binding proteins and formulated (see col. 6, line 25, col. 7, line 29; and col. 5, line 48, to col. 6, line 18).

These muscle hyperactivity diseases require a fast-acting remedy, as these are painful and debilitating conditions. Therefore, a holding of anticipation is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borodic (US 5,183,462) in view of Johnson et al. (US 5,939,070). Borodic discloses a method of treating muscle hyperactivity, comprising administering a partially purified botulinum toxin to a patient with muscle hyperactivity. See col. 1, lines 6-19 and 35-43; col. 4, lines 18-29; and the Examples in cols. 9-11. The preferred botulinum toxin is Type A, which is commercially available as a pharmaceutical preparation of known

concentration (OCULINUM), although other pharmaceutical grade preparations may be used (see col. 4, line 52, to col. 5, line 30). The muscle hyperactivity diseases that are treated include the symptoms of involuntary movements, spasms and rigid muscles (see col. 4, lines 18-29). These diseases require a fast-acting remedy, as these are painful and debilitating conditions. Borodic does not disclose that the toxin in the pharmaceutical preparation is in the fully purified form.

Johnson et al. disclose purified preparations of C. botulinum toxins that may be used to treat involuntary muscle disorders (see col. 5, lines 47-59; and col. 6, lines 10-67). Johnson et al. also disclose that *C. botulinum* toxins are produced in culture as aggregates or complexes of neurotoxin and non-toxic proteins (see col. 1, lines 10-61, and col. 2, lines 10-24). The active toxin is produced by protease cleavage of a protoxin molecule (see col. 2, lines 25-42, and col. 4, Table 2). Some of the non-toxic binding proteins have hemagglutinating ability (see col. 5, lines 47-50) and are antigenic (see col. 5, lines 54-67). It would have been obvious to one of ordinary skill in the art at the time that the invention was made to use a purified botulinum toxin composition, such as one of those of Johnson et al., e.g., purified Type A or Type B toxin (see col. 7, line 55, to col. 6, line 15; and col. 6, lines 37-59), in the method of Borodic, because Johnson et al. teach that, with a purified preparation, the active protein can exert its therapeutic effect without generating hemagglutination or an immune response in the patient (see col. 6, lines 1-10) and that a lower protein load may be administered to the patient to achieve the same effect (lower chance of an allergic reaction or other side effects). Therefore, a holding of obviousness is required.

Claims 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan (US 2001/0053369) in view of Johnson et al. (US 5,939,070). Donovan discloses a method of treating muscle hyperactivity, comprising administering a partially purified botulinum toxin to a patient with muscle hyperactivity, patients with diseases such as tremors, tics, spasms and epilepsy (see paragraphs 3-32, 40, 41, 104, 109 and 125-127). The composition containing Type A toxin contains purified neurotoxin complexes (see paragraph 35). Preparations of the other types of toxins contain these toxins in a partially purified form, as each type of toxin has been prepared in an active form and characterized (see paragraphs 39, 41 and 42). Donovan discloses that purification is necessary because, when the toxins are produced in culture, a certain amount of inactive protein containing the toxin is always present. Active toxin proteins are released by protease activity. Purification is necessary to remove the excess inactive toxin-containing molecules that increase antigenicity without contributing to clinical efficacy (see paragraph 44). Thus, these toxins are in a partially purified form, as the active proteins have been isolated from crude fermentation broth and formulated in a quantitative manner (see paragraphs 44 and 94). The muscle hyperactivity diseases that are treated include the symptoms of involuntary movements, spasms and rigid muscles (see paragraphs 8, 10, 11, 14, 21 and 26). These diseases require a fast-acting remedy, as these are painful and debilitating conditions. Donovan does not disclose that the toxin in the therapeutic preparation is in the fully purified form.

Johnson et al. disclose purified preparations of C. botulinum toxins that may be used to treat involuntary muscle disorders (see col. 5, lines 47-59; and col. 6, lines 10-

67). Johnson et al. also disclose that *C. botulinum* toxins are produced in culture as aggregates or complexes of neurotoxin and non-toxic proteins (see col. 1, lines 10-61, and col. 2, lines 10-24). The active toxin is produced by protease cleavage of a protoxin molecule (see col. 2, lines 25-42, and col. 4, Table 2). Some of the non-toxic binding proteins have hemagglutinating ability (see col. 5, lines 47-50) and are antigenic (see col. 5, lines 54-67). It would have been obvious to one of ordinary skill in the art at the time that the invention was made to use a purified botulinum toxin composition, such as one of those of Johnson et al., e.g., purified Type A or Type B toxin (see col. 7, line 55, to col. 6, line 15; and col. 6, lines 37-59), in the method of Donovan, because Johnson et al. teach that, with a purified preparation, the active protein can exert its therapeutic effect without generating hemagglutination or an immune response in the patient (see col. 6, lines 1-10) and that a lower protein load may be administered to the patient to achieve the same effect (lower chance of an allergic reaction or other side effects). Therefore, a holding of obviousness is required.

Claims 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aoki et al. (US 6,319,505) in view of Johnson et al. (US 5,939,070) and Allergan, Inc. (package insert for Botox®, http://www.botox.com/download/BotoxPI.pdf, printed on December 13, 2005). Aoki et al. disclose a method of treating muscle hyperactivity, comprising administering a partially purified botulinum toxin to a patient with muscle hyperactivity, patients with diseases involving muscle spasms (see col. 1, lines 25-35; col. 2, lines 53-64; col. 3, lines 10-14). Preparations of botulinum toxins Types A-F

contain these toxins in a partially purified form, as each type of toxin is prepared as a sterile pharmaceutical of a known activity (see col. 3, line 65, to col. 4, line 66). For example, BOTOX® or DYSPORT (Type A toxin) may be used (see col. 4, lines 59-66). Allergan discloses that Botox® is a purified neurotoxin complex (see 1st paragraph on 1st and last pages). These diseases require a fast-acting remedy, as these are painful and debilitating conditions (see col. 1, lines 14-22). Aoki et al. do not disclose that the toxin in the therapeutic preparation is in the fully purified form.

Johnson et al. disclose purified preparations of C. botulinum toxins that may be used to treat involuntary muscle disorders (see col. 5, lines 47-59; and col. 6, lines 10-67). Johnson et al. also disclose that *C. botulinum* toxins are produced in culture as aggregates or complexes of neurotoxin and non-toxic proteins (see col. 1, lines 10-61, and col. 2, lines 10-24). The active toxin is produced by protease cleavage of a protoxin molecule (see col. 2, lines 25-42, and col. 4, Table 2). Some of the non-toxic binding proteins have hemagglutinating ability (see col. 5, lines 47-50) and are antigenic (see col. 5, lines 54-67). It would have been obvious to one of ordinary skill in the art at the time that the invention was made to use a purified botulinum toxin composition, such as one of those of Johnson et al., e.g., purified Type A or Type B toxin (see col. 7, line 55, to col. 6, line 15; and col. 6, lines 37-59), in the method of Aoki et al., because Johnson et al. teach that, with a purified preparation, the active protein can exert its therapeutic effect without generating hemagglutination or an immune response in the patient (see col. 6, lines 1-10) and that a lower protein load may be administered to the patient to

achieve the same effect (lower chance of an allergic reaction or other side effects). Therefore, a holding of obviousness is required.

Claims 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Graham (US 6,395,277) in view of Johnson et al. (US 5,939,070), Allergan, Inc. (package insert for Botox®, http://www.botox.com/download/BotoxPI.pdf, printed on December 13, 2005) and Shore Laser ("Botulinum toxin for the treatment of facial lines and wrinkles," http://www.shorelaser.com/BottoxA.html, printed on December 13, 2005). Graham discloses a method of treating muscle hyperactivity due to cerebral palsy, comprising administering a partially purified botulinum toxin to a patient with muscle hyperactivity (see col. 1, lines 22-37 and 44-65; and col. 2, lines 20-42). Although any Type of botulinum toxin (A-F) may be used, the preferred embodiment is to use Type A toxin (see col. 1, lines 53-65; and col. 2, lines 15-19 and 57-60). Commercially available Type A toxin is prepared in a partially purified form, as Allergan discloses that Botox® is a purified neurotoxin complex (see 1st paragraph on 1st and last pages). Shore Laser discloses that Oculinum® is an earlier name for Botox®. Muscle hyperactivity from cerebral palsy requires a fast-acting remedy, as this is a debilitating condition that impairs the ability of the sufferer to use his muscles (see col. 1, lines 22-37). Graham does disclose that the toxin in the therapeutic preparation is in the fully purified form.

Johnson et al. disclose purified preparations of C. botulinum toxins that may be used to treat involuntary muscle disorders (see col. 5, lines 47-59; and col. 6, lines 10-

67). Johnson et al. also disclose that *C. botulinum* toxins are produced in culture as aggregates or complexes of neurotoxin and non-toxic proteins (see col. 1, lines 10-61, and col. 2, lines 10-24). The active toxin is produced by protease cleavage of a protoxin molecule (see col. 2, lines 25-42, and col. 4, Table 2). Some of the non-toxic binding proteins have hemagglutinating ability (see col. 5, lines 47-50) and are antigenic (see col. 5, lines 54-67). It would have been obvious to one of ordinary skill in the art at the time that the invention was made to use a purified botulinum toxin composition, such as one of those of Johnson et al., e.g., purified Type A or Type B toxin (see col. 7, line 55, to col. 6, line 15; and col. 6, lines 37-59), in the method of Graham because Johnson et al. teach that, with a purified preparation, the active protein can exert its therapeutic effect without generating hemagglutination or an immune response in the patient (see col. 6, lines 1-10) and that a lower protein load may be administered to the patient to achieve the same effect (lower chance of an allergic reaction or other side effects). Therefore, a holding of obviousness is required.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rosanne Kosson
Examiner, Art Unit 1653

rk/2005-12-13

ROBERT A. WAX
PRIMARY EXAMINER